11:45 a.m.

818-4 eterminants of Coronary Collateral Vessels Formation

Edmund O. Ang, Duana Walton, Kristy Breuhl, Marin Schweizer, Timothy D. Henry, *Hennepin County Medical Center, Minneapolis, Minnesota, University of Minnesota, Minneapolis, Minnesota.*

BACKGROUND: Patients with coronary collateral vessels have less myocardial ischemia and better outcome post myocardial infarction (MI) than patients without collaterals. However, there is limited information on the determinants of collateral vessels formation. We evaluated the effect of clinical, angiographic, laboratory parameters and medications on a cohort of patients undergoing coronary angiography.

METHODS: 300 consecutive patients undergoing coronary angiography were evaluated. 188 patients had coronary stenosis >75% (historically defined as sufficient for the development of coronary collateral circulation) were included in the analysis. Collateral vessel circulation was graded according to Rentrop classification and the collateral score was calculated by summing the Rentrop numbers of every patient.

RESULTS: The mean age was 58.5±11 years & 64% were male. 44% had diabetes and 49% had previous MI.

Predictors of Collateral Circulation

Predictors	Yes	No	P value
Previous myocardial infarction	1.21±1.08	0.94±1.04	0.01
Previous revascularization procedure	0.72±1	1.40±1.07	<0.001
Unstable lesion	0.94±1.04	1.26±1.13	0.01
Diabetes mellitus	0.98±0.97	1.17±1.18	0.25
>70 years old	1.01±1.09	1.10±1.91	0.53
Lipid lowering agent	0.92±1.05	1.24±1.10	0.008
Aspirin	1.14±1.08	0.81±1.11	0.01

CONCLUSIONS: Collateral vessels was more apparent in patients with previous MI and patients on aspirin. In contrast, patients with unstable presentation, previous revascularization and those on lipid lowering agent had lower Rentrop scores. Diabetes and age were not predictive. In addition, collateral development was more frequent in patients with occluded or subtotal lesions. Development of coronary collateral vessels is a complex process and the determinants in an individual patient require further study as we investigate new therapeutic options to stimulate coronary angiogenesis.

Noon

818-5 Prognostic Impacts of Practical Assessment for Microvascular Coronary Vasomotor Dysfunction

Tatsuaki Murakami, Kazuo Ohsato, *Fukui Cardiovascular Center, Fukui, Japan.*

Background. Although microvascular coronary vasomotor dysfunction (VMD) is thought to contribute to coronary atherothrombosis, there has been little practical evidence for the relationship. This study investigated whether practically evaluated VMD has prognostic impacts.

Methods. VMD was graded by 2 variables: (1) the endothelium-independent flow increases to infusion of ATP (50μg) (FN), and (2) the endothelium-dependent increases to infusion of acetylcholine (50μg) (FE) into the normal or minimally diseased (%-diameter stenosis <30%) left coronary artery using quantitative coronary arteriography and doppler-wire in consecutive 150 patients with suspected coronary artery disease. The patients were categorized into tertile groups according to the values of FN and FE, and we prospectively followed-up their major adverse coronary events (MACE: cardiac death, CABG, heart failure, non-fatal acute coronary syndrome).

Results. For a mean follow-up period of 64 months (range; 58 to 81) with 100% follow-up, the patients in the lower third with severe VMD (Group-L) of 2 variables more frequently developed MACE (Group-L versus Group-M with mild VMD plus Group-H with normal vasomotor function, by Kaplan-Meier analysis). All patients with MACE belonged to Group-L of FN or FE. Cox proportional analysis showed severe VMD of FN or FE was an independent predictor for MACE.

Conclusion. These results suggest evaluation of microvascular coronary vasomotor function highly predicts future coronary events.

	Group-L	Group-M	Group-H
FN	12 (24%)	3 (6%)	3 (6%)
FE	14 (28%)	3 (6%)	1 (2%)

ORAL CONTRIBUTIONS

821 Vasoactive Hormones and Receptors in Cardiovascular Disease

Monday, March 18, 2002, 11:00 a.m.-12:15 p.m.
Georgia World Congress Center, Room 367W

11:00 a.m.

821-1 Potent Cardiac Unloading Actions of a New Synthetic Natriuretic Peptide (BD-NP) in Experimental Severe Congestive Heart Failure

Guido Boerrigter, Lisa C. Costello, Ondrej Lisy, Alessandro Cataliotti, Toshihiro Tsuruda, Gail J. Harty, John C. Burnett, Jr., *Mayo Clinic and Foundation, Rochester, Minnesota.*

Background: Natriuretic peptides (NPs) play an important role in cardiorenal homeostasis. BNP has been approved for the treatment of acute heart failure. DNP was first identified in the green mamba snake and due to its long C-terminus may be more resistant to enzymatic degradation by neutral endopeptidase. We designed and synthesized a new NP by combining the ring structure and N-terminus of BNP with the extended C-terminus of DNP. We assessed the cardiorenal actions of this chimeric BD-NP in a model of severe congestive heart failure (CHF).

Methods: Severe CHF was induced in 7 dogs by rapid ventricular pacing (240 bpm) for 10 days. Cardiorenal parameters were assessed in 30-minute clearances at baseline, with low dose (10 ng/kg/min) and high dose (50 ng/kg/min) BD-NP infusion, and after a washout period of 30 minutes (post infusion). Values are expressed as mean±SEM; *p<0.05 vs. Baseline.

Results: Administration of low and high dose BD-NP decreased right atrial pressure (from baseline 3.3±2.2 to 2.0±2.1* and -0.1±2.1* mm Hg), pulmonary artery pressure (from 22±3 to 19±3* and 16±3* mm Hg), and pulmonary capillary wedge pressure (15±3 to 12±3* and 10±3* mm Hg). Mean arterial pressure, cardiac output, and systemic vascular resistance remained unchanged. Urine flow (from 0.22±0.09 to 0.49±0.13 and 1.07±0.16* mL/min) and urinary sodium excretion (26±14 to 70±20 and 195±29* μEq/min) increased. Renal blood flow (from 47±5 to 54±5 and 64±6* mL/min) and glomerular filtration rate (GFR) (from 27±5 to 35±7 and 57±9* mL/min) increased. Plasma cGMP (from 19±2 to 28±2* and 39±4* pmol/mL) and urinary cGMP excretion (from 1742±296 to 3472±583 and 9658±3362* pmol/min) markedly increased, whereas plasma renin activity (from 6.6±2.2 to 4.8±1.8 and 3.2±1.4* ng/mL/h) and angiotensin II (from 81±29 to 24±10* and 10±3* pg/ml) decreased. These beneficial effects were sustained in the post infusion clearance.

Conclusion: The new chimeric natriuretic peptide BD-NP decreases cardiac filling pressures, is diuretic and natriuretic, enhances GFR, and suppresses the renin-angiotensin system. Further studies are warranted to assess the therapeutic potential of this unique designer peptide in cardiorenal disease.

11:15 a.m.

821-2 Renoprotective Effect of Chronic Adrenomedullin Infusion in Dahl Salt-Sensitive Rats

Toshio Nishikimi, Naihiko Kobayashi, Yosuke Mori, Kazuyoshi Tadokoro, Xing Wang, Kazumi Akimoto, Kenji Kangawa, Hiroaki Matsuoka, *Dokkyo University School of Medicine Medicine, Medlocine, Mlbu, Tochigi 321-0293, Japan, National Cardiovascular Center, Osaka, Japan.*

Background: Adrenomedullin (AM) is a potent vasodilatory and natriuretic peptide that plays an important role in pathophysiology of cardiovascular disease. Recent studies demonstrated that AM has inhibitory effect of proliferation and DNA synthesis in mesangial cells, vascular smooth muscle cells, and endothelial cells in vitro. However, whether administration of AM has renoprotective effect in vivo remains unknown.

This study was designed to examine whether chronic AM infusion has renoprotective effects in hypertensive rats.

Methods: Human recombinant AM (500ng/h) or vehicle was infused for approximately 7 weeks by osmotic minipump in 11-week-old Dahl salt-sensitive rats (DS-AM, n=9; DS-cont, n=9). Dahl salt-resistant rats were used as a control (DR, n=9). After 7 weeks of treatment, blood pressure, renal function, histological findings, hormone levels, and renal molecular markers were measured.

Results: DS-cont was characterized by decreased kidney function, impaired histological findings, altered hormone levels, and altered renal molecular markers. Chronic AM treatment significantly improved renal function (serum Cre: -87%, serum BUN: -73%, CCr: +114%, urinary protein excretion: -59%) without changing mean arterial pressure (-4%). Histological examination revealed that chronic AM infusion significantly improved glomerular injury score (-54%). Chronic AM treatment significantly inhibited increase of endogenous plasma rat AM levels (-97%), plasma renin concentration (-269%), aldosterone levels (-82%) and decreased tissue angiotensin II levels both in renal cortex and medulla(-60%, -93%). Furthermore, AM infusion significantly decreased mRNA expression of TGF-beta both in renal cortex and medulla (-63%, -115%), ACE both in renal cortex and medulla (-137%, -79%), renin both in renal cortex and medulla (-230%, -134%), and increased mRNA expression of AT1-receptor in renal cortex (+46%).

Conclusion: These results suggest that chronic AM infusion has renoprotective effects in this type of hypertension model, at least in part, via inhibition of circulating and renal tissue renin-angiotensin system.